UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/247,886	02/10/99	PUNNONEN J	18097-030200

022798 HM12/0620
LAW OFFICES OF JONATHAN ALAN QUINE
P O BOX 458
ALAMEDA CA 94501

EXAMINER	
CHEN, S	
ART UNIT	**PAPER NUMBER**
1633	16

DATE MAILED: 06/20/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/247,886	PUNNONEN ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23 and 51-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23 and 51-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Applicants' amendment filed 4-17-01 has been entered. Claims 24-50 has been canceled. Claims 1-5, 7, 8, 10, 12-19, 22, 23, 51, 53-58 have been amended. Claims 59-64 have been added.

Claims 51-58 have been rejoined with claims 1-23 for examination after reconsideration of the subject matter of claims 51-58. Thus, claims 1-23 and 51-64 are pending and under consideration.

Claim Objection

Claims 15 and 16 are objected because they are duplicate claims. Claims 15 and 16 both are directed to a composition for eliciting an immune response that comprises a cell-specific recombinant binding moiety obtained by the method of claim 2. Appropriate correction is required.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 2-23 and 51-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "recombining **at least first and second forms** of **at least one** nucleic acid which comprises a polynucleotide that encodes a nucleic acid binding domain" in claim 2 section (1) is vague and renders the claim indefinite. It is unclear which form of nucleic acid encodes a nucleic acid binding domain or whether another form of nucleic acid encodes a nucleic acid binding domain. Similarly, the phrase "**at least first and second forms** of **at least one** nucleic acid which comprises a polynucleotide that encodes a cell-specific ligand" in claim 2 is vague and renders the claim indefinite. It is unclear which form of nucleic acid encodes a cell-specific ligand or whether another form of nucleic acid encodes a cell-specific ligand.

The phrase "one or more members of a **library of vectors**" in claim 2 section (2) and claim 3 section (7) is vague and renders the claim indefinite. There is no antecedent basis for the "library of vectors". It is unclear what "library of vectors" is intended.

The phrase "binding the expressed recombinant binding moiety to a vector" in claim 2 section (3) and claim 3 section (8) is vague and renders the claim indefinite. It is unclear where the "expressed recombinant binding moiety" comes from because the "expressed recombinant binding moiety" has not been recovered from the transfected host cells.

The phrase "determining if one or more target cells contains **a vector**" in claim 2 section (5) and claim 3 section (9) is vague and renders the claim indefinite. It is unclear what "vector" is

intended, is it the "vector-binding moeity complex" or any other "vector"? Claims 3-15 and 60-63 depend on claim 2 and fail to clarify the indefiniteness set forth above.

The phrase "recombining **at least first and second forms** of **at least one** nucleic acid that comprises a polynucleotide that encodes a binding moiety of an enterotoxin" in claim 18 section (1) is vague and renders the claim indefinite. It is unclear which form of nucleic acid encodes a binding moiety of an enterotoxin or whether another form of nucleic acid encodes a binding moiety of an enterotoxin.

The phrase "one or more members of a **library of vectors**" in claim 18 section (2) is vague and renders the claim indefinite. There is no antecedent basis for the "library of vectors". It is unclear what "library of vectors" is intended.

The phrase "contacting the recombinant cell-specific binding moiety polypeptide with a cell surface receptor" in claim 18 section (3) is vague and renders the claim indefinite. It is unclear where the "recombinant cell-specific binding moiety polypeptide" comes from because the "cell-specific binding moiety polypeptide" has not been recovered from the transfected host cells. Claims 19-23 depend on claim 18 and fail to clarify the indefiniteness set forth above.

The phrase "vaccine antigen" in claims 51, 53 and 64 is vague and render the claim indefinite. A "vaccine antigen" could be a DNA, RNA, a peptide, a polypeptide, a polysaccharide, or any molecule or cell that can stimulate an immune response in a host for vaccination purpose. It is unclear what type of "vaccine antigen" is intended in the present

application. The specification fails to specifically define the phrase "vaccine antigen". Claims 52 and 54-58 depend on claim 51 and fail to clarify the phrase "vaccine antigen".

The phrase "in at least on form of at least one nucleic acid of (1)" in claim 59 line 2 is vague and renders the claim indefinite. It is unclear what the phrase "in at least on form of at least one nucleic acid of (1)" mean and what is intended to be claimed.

In general, the method claims are indefinite because there is a disconnect between the steps of the method. The subsequent steps of the method do not follow from the previous step such that the material used is not provided for elsewhere in the claims. Each claim should be thoroughly reviewed for definiteness.

Claim 17 is indefinite because the phrase "a polynucleotide sequence that is capable of expressing an antigen comprises a binding site" is unclear. The phrase is grammatically incorrect. It should be re-worded to point out that the polynucleotide expresses an antigen and comprises the binding site delineated by the claim.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 51-58 and 64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing and screening a cell-specific

binding moiety nucleic acid, containing a nucleic acid encoding a nucleic acid binding domain and a cell-specific ligand that specifically binds to the surface of the target cell, useful for increasing uptake or specificity of a genetic vaccine for a target cell and the expressed binding moiety polypeptide can bind to a polynucleotide sequence comprising the binding site for said nucleic acid binding domain, does not reasonably provide enablement for a method of producing and screening the cell-specific binding moiety that could fuse to, link to, or coat on any vaccine antigen other than the polynucleotide comprising the nucleic acid binding site. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 51-58 and 64 are directed to a method for producing and screening a cell-specific binding moiety polypeptide useful for increasing uptake or specificity of a vaccine antigen for a target cell by recombining at least first and second forms of a nucleic acid encoding a cell specific binding moiety to create a library of recombinant binding moiety-encoding nucleic acids, expression of said recombinant binding moiety, to screen the optimized recombinant cell-specific binding moiety polypeptide, and to fuse, link, or coat the recombinant cell-specific binding moiety polypeptide to a vaccine antigen.

The claims encompass any type of vaccine antigen that includes a DNA, RNA, a peptide, a polypeptide, a polysaccharide, or any molecule or cell that can stimulate an immune response in a host for vaccination purpose. The cell-specific binding moiety encoded by a polynucleotide encompasses binding activity to a polynucleotide or a polypeptide. The specification of the

present application only teaches the binding of a cell-specific binding moiety containing a nucleic acid binding domain to a polynucleotide comprising a binding site for said nucleic acid binding domain. The specification fails to provide adequate guidance and evidence for fusing, linking, or coating of a cell-specific binding moiety to any vaccine antigen other than the polynucleotide sequence set forth above. It is unclear how a cell-specific binding moiety polypeptide, having any binding activity, would fuse to, link to, or coat on a DNA, RNA, a polypeptide, a polysaccharide, or any molecule or cell that can stimulate an immune response in a host for vaccination. It is understood that the utility of the cell-specific binding moiety produced and screened by the claimed method is to provide a more efficient carrier for an antigen to obtain efficient vaccination. Absent the teachings of fusing, linking, or coating the binding moiety polypeptide to any DNA, RNA, any polypeptide, any polysaccharide, or any molecule or cell that can stimulate an immune response in a host for vaccination, one skilled in the art at the time of the invention would not know how to use the claimed invention and require undue experimentation to practice over the full scope of the invention claimed.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 14-16 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stemmer et al. 1997 (AG) in view of Ledley et al., 1994 (AH) and Patten et al., 1997 (BG).

Claim 1 is directed to a method for producing and screening a cell-specific binding molecule useful for increasing uptake or specificity of a genetic vaccine for a target cell by recombining at least first and second forms of a nucleic acid encoding a nucleic acid binding domain and a cell-specific ligand that specifically binds to the surface of the target cell to create a library of recombinant binding moiety-encoding nucleic acids and to screen the optimized recombinant cell-specific binding moiety nucleic acids. Claim 14-16 and 58 are directed to a cell specific recombinant binding moiety produced by the method set forth above and a composition containing said cell-specific recombinant binding moiety.

Stemmer teaches a method for the production of nucleic acid fragments or polynucleotides encoding mutant proteins by repeated cycles of mutagenesis, shuffling and selection of nucleic

acids to generate polynucleotides having desired characteristic by iterative selection and recombination for the molecular evolution *in vitro* or *in vivo* of proteins (e.g. abstract). Stemmer teaches a method of evolving a polynucleotide sequence toward a desired property comprising recombining at least a first and second forms of the polynucleotide sequence to produce a library of recombinant forms of the sequence, screening at least a first recombinant sequence from said library, recombining said first recombinant sequence with a further form of the polynucleotide sequence, the same or different from the first and second forms, to produce a further library, and screening at least one further recombinant polynucleotide from said further library (e.g. p.164).

Stemmer does not teach generating a chimeric recombinant DNA comprising a DNA binding domain and a ligand which binds to the surface of a target cell.

Ledley teaches generating a chimeric recombinant DNA-binding protein comprising a first element for binding to a receptor on a target cell and a second element required for binding to DNA, such as histone or transacting regulatory element, and a complex for gene transfer comprising a DNA molecule specifically and non-specifically bound to the chimeric recombinant DNA-binding protein (e.g. p. 26, 27, abstract).

Patten teaches "viral vaccine vectors can be enhanced by DNA shuffling to give desired properties of tropism, stability and expression level", and DNA shuffling could be a tool " for increasing the efficiency and success rate of the development of novel whole organism, viral, bacterial and recombinant protein vaccines" (e.g. p. 732).

It would have been obvious for one of ordinary skill in the art at the time of the invention to substitute the first and second forms of polynucleotide sequences taught by Stemmer with polynucleotide sequences encoding a DNA-binding element and a ligand binding to a receptor on a target cell as taught by Ledley for the production of a genetic vaccine as taught by Patten.

One having ordinary skill at the time of the invention would have been motivated to do so because the generation of a chimeric recombinant DNA-binding protein comprising a first element for binding to a receptor on a target cell and a second element required for binding to DNA could facilitate the efficiency of gene transfer and the effects of a genetic vaccine to stimulate immune response in a host.

It should be noted that the method of making a composition does not carry weight in the 103(a) rejection of the composition claims.

Applicants argue that Ledley and Patten do not teach or suggest "creating a library of recombinant polynucleotides" by recombining a nucleic acid encoding one function with another nucleic acid encoding a different function (amendment, page 16). This is not found persuasive because Stemmer teaches a method of evolving a polynucleotide sequence toward a desired property comprising recombining at least a first and second forms of the polynucleotide sequence to produce a library of recombinant forms of the sequence, screening at least a first recombinant sequence from said library, recombining said first recombinant sequence with a further form of the polynucleotide sequence, the same or different from the first and second forms, to produce a

further library, and screening at least one further recombinant polynucleotide from said further library. The collective teachings of Stemmer, Ledley, and Patten would provide motivation for one of ordinary skill in the art at the time of the invention to practice the claimed invention in claim 1.

Conclusion

Claims 1-23 and 51-64 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark can be reached on (703) 305-4051. The fax phone number for this group is (703) 308-4242.

Questions of formal matters can be directed to the patent analyst, Kimberly Davis, whose telephone number is (703) 305-3015.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Deborah Clark

DEBORAH J. R. CLARK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600